Journal of Exposure Analysis and Environmental Epidemiology (2000) 10, 206–209

www.nature.com/jea

A comparison of recent and long-term average measurements of nitrate in drinking water

D. MICHAL FREEDMAN,[a] KENNETH P. CANTOR,[b] MARY H. WARD[b] AND KATHY J. HELZLSOUER[c]

[a]*Radiation Epidemiology Branch, National Cancer Institute, 6120 Executive Boulevard, Bethesda, Maryland*
[b]*Occupational Epidemiology Branch, National Cancer Institute, 6120 Executive Boulevard, Bethesda, Maryland*
[c]*The Johns Hopkins University, School of Hygiene and Public Health, Department of Epidemiology, 615 North Wolfe Street, Baltimore, Maryland*

We evaluated the usefulness of a recent measure of drinking water nitrate as a predictor of long-term average nitrate exposure calculated from historic data. Exposure estimates were calculated for 214 study participants who used public water supplies between 1947 and 1980 in Minnesota. Long-term average nitrate was calculated by linking residential histories to historical nitrate data. For recent exposures, we averaged nitrate measurements in 1980, or the next closest year with measurements. The Spearman correlation coefficient for the relationship between the two measures was 0.54 (95% confidence interval [CI] = 0.44–0.63). Agreement was highest among those residing 34 or more years in their town as of 1980 (r_s = 0.70; 95% CI = 0.55–0.80). These findings suggest that taking into account the study participants' duration of residence may enhance the validity of using a recent measure as an indicator of past exposures. *Journal of Exposure Analysis and Environmental Epidemiology* (2000) **10**, 206–209.

Keywords: *cancer, measurement, nitrate, non-Hodgkin's lymphoma, water.*

Introduction

Long-term exposure to elevated levels of nitrate in drinking water has been suggested as a possible risk factor for non-Hodgkin's lymphoma (NHL) (Ward et al., 1996), stomach cancer (Cuello et al., 1976), brain cancer (Barrett et al., 1998), and diabetes (Parslow et al., 1999). Some studies of the health effects of nitrate have used nitrate exposure data from the recent past as a surrogate for long-term estimates (Rademacher et al., 1992; Heckman et al., 1997; Barrett et al., 1998; Law et al., 1999; Parslow et al., 1999). The degree to which recent measurements estimate long-term nitrate exposure measurements, however, has not been examined.

In a recent study of nitrate in drinking water and NHL in Minnesota (Freedman et al., 2000), we used historical records of nitrate in public drinking water over several decades and linked them to individual lifetime residential histories to estimate long-term average exposure to nitrate. In the current study, we examine how well recent measurements of exposure to nitrate in drinking water in Minnesota reflect these long-term average exposures. We also examine whether subgroup analysis could aid in reducing misclassification that results from using recent measurements.

1. Address all correspondence to: Dr. D. Michal Freedman, PhD, National Cancer Institute, Radiation Epidemiology Branch Room 7087, EPS 6120 Executive Boulevard Bethesda, MD 20892-7238. Tel.: (301)594-7163. Fax: (301)402-0207. E-mail: mf101e@nih.gov
Received 11 August 1999; accepted 29 December 1999.

Methods

The study population in these analyses were participants in a population-based case–control study of NHL undertaken from 1980 to 1984 and designed to study agricultural and other risk factors for NHL and leukemia in Minnesota (Cantor et al., 1992). We restricted the analysis to those who used Minnesota public water supplies for more than 90% of the years between 1947 and 1980 to limit nitrate exposure misclassification by unknown levels in private wells. We also only included those who reported using a Minnesota public water supply in 1980 to permit calculation of an exposure estimate for 1980. This resulted in a total of 71 cases and 143 controls who used water supplies from more than 150 communities in Minnesota. We obtained records of nitrate measurements (based on nitrate as nitrogen) in Minnesota public water supplies from the Minnesota Department of Health (MDH) for the period 1947 through 1984. Details of the original study design and general data collection methods are described elsewhere (Cantor et al., 1992).

To estimate the study participants' long-term average exposure to nitrate in drinking water, we linked the participants' residential history to estimated annual nitrate levels in the drinking water of each community of residence identified. As a first step, we calculated annual nitrate levels in the drinking water of each community between 1947 and 1975. When a community used ground water, as most Minnesota communities do, we used nitrate measurements from both public wells and public distribution points (which reflect the mix of water from operating public wells). For any nitrate value identified as non-detectable, we assigned a value one-half the detection threshold to limit misclassification. We summed nitrate and nitrite measurements for the same source made at the same time in both well and distribution point sources because laboratory reports often included a combined measure and the nitrite in ground water and surface water is negligible as compared with nitrate levels (National Research Council, 1995).

Nitrate measurements, which were sparse in the late 1940s, became more frequent over time. About 76% of communities had nitrate measurements in the period 1947 through 1959 compared to 95% in the last decade, 1970 through 1979.

To fill in years with missing data and use all available information in estimating exposure in years where measurements had been made, we calculated a time-weighted nitrate average for each year in each community. Measurements within 2 years of the year being estimated were weighted as 1; from more than 2–5 years, as 0.5; from more than 5–10, as 0.2. Measurements more than 10 years away were weighted as 0.01 to ensure an estimate for early years (when some towns had no records), but prevent undue weight to be given to measures distant in time if measurements closer in time existed. Because distribution point measurements reflected actual tap water delivered to community residents, in years when two distribution point measurements were made, we used their average as the final estimate for that year, and gave double weight to distribution point measurements in estimating concentrations for all other years in the algorithm.

We linked the participants' reported residential history with the estimated nitrate level by year in each community of residence. For any year in which participants reported using bottled water, we assumed the nitrate level to be zero. Bottled water use accounted for less than 1% of all person years. We then calculated an estimated arithmetic average nitrate exposure for cases and controls for the period 1947 through 1975, which allowed for a 5-year lag period from 1980, the earliest diagnosis date.

In contrast, we calculated recent nitrate exposure by averaging all measurements in each participant's town or residence for 1980, or if no measurements were available in 1980, we averaged measurements from the closest year when measurements were available. Ninety-nine percent of the measurements used to calculate recent nitrate exposure was within 3 years of 1980.

Table 1. Spearman rank correlation coefficients and 95% CIs between long-term average and the recent nitrate exposure measure[a], stratified by demographic and other characteristics.

Characteristics	Number (%)	Median (interquartile range) of long-term average measure[b]	Median (interquartile range) of recent measure[c]	Correlation coefficient (r_s) (95% CI)
Age in 1980				
≤60	51 (24)	0.5 (0.4–0.9)	0.3 (0.2–1.6)	0.63 (0.43–0.77)
61–75	96 (45)	0.5 (0.3–0.6)	0.2 (0.2–0.5)	0.49 (0.32–0.63)
≥76	67 (31)	0.5 (0.3–0.8)	0.3 (0.2–0.8)	0.46 (0.25–0.63)
Ever-farmer				
Yes	71 (33)	0.5 (0.4–0.8)	0.3 (0.2–1.1)	0.61 (0.44–0.74)
No	143 (67)	0.5 (0.3–0.7)	0.3 (0.2–0.6)	0.49 (0.35–0.61)
Years of education				
≤12 or vocational	160 (75)	0.5 (0.4–0.8)	0.3 (0.2–0.7)	0.52 (0.40–0.62)
>12	54 (25)	0.5 (0.3–0.8)	0.2 (0.2–0.7)	0.57 (0.36–0.73)
Years in 1980 residence[d] as of 1980				
≤9	46 (21)	0.4 (0.3–0.5)	0.2 (0.2–0.4)	0.17 (0–0.44)
10–20	49 (23)	0.5 (0.4–0.7)	0.3 (0.2–0.5)	0.44 (0.18–0.64)
21–33	52 (24)	0.5 (0.4–0.8)	0.3 (0.2–1.4)	0.63 (0.43–0.76)
≥34	67 (31)	0.5 (0.4–0.7)	0.4 (0.2–0.8)	0.70 (0.55–0.80)

[a]Study participants with (1) ≥90% years 1947–1980 with public water supplies in Minnesota; and (2) reported use of Minnesota public water in 1980.
[b]"Long-term average" measure is based on nitrates measured in public water supplies in 1947–1975.
[c]"Recent" measure is based on an average of measurements in 1980 or in the closest year when measurements were available.
[d]"1980 residence" refers to the town participants identified as where they resided.

We calculated the Spearman's rank order correlation coefficient for the relationship between the average long-term and the recent nitrate measures for cases and controls combined. Spearman's correlation was used because the two measures were not normally distributed (Altman, 1991). We looked at the combined population because in the study on which this analysis is based (Freedman et al., 2000), case status was unrelated to long-term average nitrate estimates. We also calculated the Spearman correlation coefficients for strata of age, farming status, education, and residential history. All stratification variables were examined as of 1980.

Results

The median age for the study population was 70 years, with a range of 31–95 years. Fifty percent of the study population have lived in their 1980 residence for at least 24 years.

The median of the recent nitrate measure was lower than the median of the long-term average measure (0.3 mg/l; *cf.* 0.5 mg/l). The Spearman rank correlation coefficient for the relationship between the recent and long-term average exposure was 0.54 (95% confidence interval [CI]=0.44–0.63).

Table 1 shows the medians and interquartile range of the two measures and the Spearman rank correlation matrix for subpopulations stratified by age, farming status, education, and duration of the participant's 1980 residence. The medians of the recent measures generally were slightly lower than the long-term average measure (maximum difference=0.3 mg/l). Except for duration of residence, the correlation coefficients were between 0.46 and 0.63. The coefficients were lower among those who have lived in their 1980 residences for 20 years or less (r_s=0.17 for ≤9 years and r_s=0.44 for 10–20 years), and highest among those who have resided longest in their residence (r_s=0.70 for ≥34 years).

Discussion

This study compared a recent measure of nitrate exposure, which sometimes may be the only available measure, with an estimate of historical nitrate exposure. Many factors could explain a difference between recent and historical nitrate exposures, even where residence remains unchanged and nitrate levels in ground water have remained constant. These include a replacement or discontinuation in the use of particular wells and changes in the blending of water from multiple wells.

In this study, the overall Spearman rank order correlation of 0.54 between the two measures was fair. This level of agreement is comparable to the correlations found in studies comparing food frequency questionnaires and dietary records, which generally range between 0.4 and 0.7 (Willett, 1994).

One factor that is unrelated to actual nitrate concentrations but that may have adversely affected the correlation between recent and long-term averages is the changing detection limits for waterborne nitrate over time. These decreased from a general limit of 1 mg/l prior to about 1975, to 0.4 mg/l after about 1975. Therefore, some low nitrate levels used to calculate recent exposure were lower than measurements for similar historic nitrate levels used to calculate long-term exposure.

The generalizability of the study may also have been limited by the unexpectedly narrow range of exposures in the Minnesota study population. The narrow exposure range was likely due, at least in part, to our use of public water supplies, which are monitored and regulated for nitrate levels.

Despite these limitations, the stratified analysis in Table 1 suggests a group within the population for whom the short-term measure provides better agreement, particularly for those using public water supplies. The correlation between nitrate measures was strongest (r_s=0.70) among those study participants who had the most stable residential histories (34 or more years at their 1980 residence). Table 1 also indicates that the correlation was poor among those who had relatively unstable residential histories (<10 years in 1980 residence). These findings are consistent with a study of trihalomethane exposure estimates that found that correlations between the most recent trihalomethane levels and lifetime estimates were strongest among those with long residency in their current residence (Cantor et al., 1998).

Lifetime exposure estimates reflect water variability due to historical changes in each sources, as well as the multiplicity of sources supplying the various residential locations in a person's life. The higher correlation among those with stable residential histories likely reflects the elimination of one source of variability — the location of the water source.

Conclusion

While there are uncertainties to generalizing from these results, they suggest that among those with long-term residence in their current town, the agreement between average long term and recent measures may be moderately good. Thus, epidemiologic studies that use recent measures of nitrate exposure as a surrogate for longer-term exposure measures may reduce exposure misclassification by taking into account variability due to an unstable residential history. This could include stratifying the study population by residential duration or restricting the study population to those with long-term residence in their current residence.

Acknowledgments

We thank the participants of the study for their contributions; the staff of the Minnesota Department of Health, particularly Jerry Smith and Jean Kahilianen, for general guidance and assistance with the data; Bob Banks of IMS for programming support; Lucy Bill of Westat, and Casey Boudreau and Diane Gezelter of SRA for their contributions to the collection and preparation of data; Paul Strickland, Adolfo Correa, Marie Diener-West, and George W. Comstock of the Johns Hopkins School of Hygiene and Public Health for their comments; and Jay Lubin of the National Cancer Institute for statistical advice.

References

Altman D.G. Relation between two continuous variables. In: Practical Statistics for Medical Research. Chapman & Hall, New York, 1991, pp. 277–324.

Barrett J.H., Parslow R.C., McKinney P.A., Law G.R., and Forman D. Nitrate in drinking water and the incidence of gastric, esophageal, and brain cancer in Yorkshire, England. *Cancer Causes Control* 1998: 9: 153–159.

Cantor K.P., Blair A., Everett G., et al. Pesticides and other agricultural risk factors for non-Hodgkin's lymphoma among men in Iowa and Minnesota. *Cancer Res.* 1992: 52: 2447–2455.

Cantor K.P., Hildesheim M.E., Freedman D.M., and Lynch C.F. Comparison of cancer risk estimates using recent and lifetime measures of exposure to drinking water contaminants. *Epidemiology* 1998: 9: S78.

Cuello C., Correa P., Haenszel W., et al. Gastric cancer in Colombia: suspect environmental agents. *J. Natl. Cancer Inst.* 1976: 57: 1015–1020.

Freedman D.M., Cantor K.P., Ward M.H., and Helzlsouer K. A case–control study of nitrate in drinking water and non-Hodgkin's lymphoma in Minnesota. *Arch. Environ. Health* 2000, in press.

Heckman C.W., dos Campos J.L.E., and Hardoim E.L. Nitrite concentration in well water from Pocone, Mato Grosso, and its relationship to public health in rural Brazil. *Bull. Environ. Contam. Toxicol*. 1997: 58: 8–15.

Law G., Parslow R., McKinney P., and Cartwright R. Non-Hodgkin's lymphoma and nitrate in drinking water: a study in Yorkshire, United Kingdom. *J. Epidemiol. Community Health* 1999: 53: 383–384.

National Research Council. Nitrate and Nitrite in Drinking Water. National Academy Press, Washington, DC, 1995, pp. 1–63.

Parslow R.C., McKinney P.A., Law G.R., Staines A., Williams R., and Bodansky H.J. Incidence of childhood diabetes mellitus in Yorkshire, northern England, is associated with nitrate in drinking water: an ecological analysis. *Diabetologia* 1999: 40: 550–556.

Rademacher J.J., Young T.B., and Kanarek M.S. Gastric cancer mortality and nitrate levels in Wisconsin drinking water. *Arch. Environ. Health* 1992: 47: 292–294.

Ward M.H., Mark S.D., Cantor K.P., Weisenburger D.D., Correa-Villasenor A., and Zahm S.H. Drinking water nitrate and the risk of non-Hodgkin's lymphoma. *Epidemiology* 1996: 7: 465–471.

Willett W. Future directions in the development of food-frequency questionnaires. *Am. J. Clin. Nutr.* 1994: 59 (suppl): 171s–174s.